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A Rare Presentation of Acute Abdomen with Perforated GIST of the Small Bowel: Surgical Management and Adjuvant Therapy- Case Report with Literature Review

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دراسة حالة نادرة مع مراجعة الأدبيات لمريض بطن حادة نتيجة إنفجار ورم النسيج السدوى الهضمى:العلاج الجراحى والعلاج المساند

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Abstract:

Background: Gastrointestinal stromal tumors (GISTs) are the major mesenchymal tumors of the gastrointestinal tract (GIT), which progress due to the mutation in TKI and PDGFR-α receptors. It shows asymptomatic conditions however, become malignant due its large size and produce abdominal pain. Several surgical managements have been applied to diagnose patients with GIST, but these increase the risk of tumor recurrent rate. Therefore, adjuvant therapies contribute to preventing this challenge with several side effects and post-operative complications. A 42-year-old male patient from Libya with acute abdomen and GIST in small bowel (Jejunum) was diagnosed with complete excision besides lymph node dissection..**Aim:** To investigate numerous case reports through literature analysis regarding GIST along with a case presentation of the patient. **Method:** This research employed a literature-based study design. Previous case reports were screened from various online research platforms, including the National Center for Biotechnology Information (NCBI) and PubMed. A total of 37 cases were included through the search phrase "Case report on Gastrointestinal stromal tumor" .. **Results:** The findings revealed patient mean age (56.35) with most of the small intestine GIST (6.42 cm) site of origin, antibodies expression, and maximum mitotic cell counts.. **Conclusion:** The cases reported a risk of recurrence among GIST patients due to high mitotic counts and tumor size. Future researchers should address immune markers to reduce tumor recurrence among GIST patients. Stakeholders should implement proper treatment procedures with effective diagnostic methods.

Keywords: Gastro-Intestinal Stromal Tumors (GISTs), Perforation, Imatinib, Acute abdomen, Tyrosine Kinase Inhibitor (TKI), Small Bowel.

الملخص:

الخلفية البحثية: أورام النسيج السدوى المعدى المعوى(تجى آى إس تى)تعتبر من الأورام الميزانشيمية المتوسطية الرخوة الرئيسية فى الجهاز الهضمى وتنشأ نتيجة طفرة جينية فى مستقبلات تى كى آى وبى دى تجى إف آر-ألفا. هى غالبا ماتكون بدون أعراض لكنها قد تتحول إلى أورام خبيثة بسبب حجمها الكبير مما يؤدي إلى ألم بطني. تم تطبيق عدة أساليب جراحية لتشخيص وعلاج مرضى (تجى آى إس تى) إلا أن هذه الأساليب قد ترفع خطر تكرار الورم. لذلك تساهم العلاجات المساندة في الحد من هذه المشكلة، لكنها قد تسبب آثارًا جانبية ومضاعفات بعد العملية. المقال يقدم مريض يبلغ من العمر 42عام من ليبيا وصل بحالة بطن حاد وتم تشخيصه بورم النسيج السدوى المعدى المعوى فى الأمعاء الدقيقة(الصائم) مع ثقب وإنفجار داخل التجويف البطنى وتم إستئصال الورم بالكامل مع إستئصال العقد الليمفاوية المحيطة.. **الهدف:** التحقيق في عدد من التقارير المنشورة عن حالات مشابهة من خلال مراجعة الأدبيات العلمية المتعلقة بمرضى تجى آى إس تى إضافة إلى عرض حالة المريض ضمن هذه الدراسة.. **الطريقة:** استخدم هذا البحث تصميمًا دراسيًا قائمًا على مراجعة الأدبيات. تم فحص تقارير الحالات السابقة من منصات بحثية إلكترونية متنوعة، بما في ذلك المركز الوطني لمعلومات التقانة الحيوية(إن سى بى آى) وقاعدة بيانات بب ميد. تم تضمين 37 حالة في المجمل من خلال البحث باستخدام عبارة "تقرير حالة عن ورم سدوي معدي معوي".. **النتائج:** أظهرت النتائج عن متوسط عمر المرضى كان (56.35) مع معظم موقع منشأ ورم الجهاز الهضمي في الأمعاء الدقيقة ومتوسط حجم الورم كان (6.42 سم)، وتم دراسة التعبير عن الأجسام المضادة، والحد الأقصى لعدد الخلايا الانقسامية.. **الخلاصة**: تشير الحالات المُبلغ عنها إلى وجود خطر انتكاس المرض لدى مرضى أورام الجهاز الهضمي السدوية نتيجة

ارتفاع معدل الانقسام الخلوي وحجم الورم. مما ينبغي على الباحثين في المستقبل التركيز على المؤشرات المناعية للحد من انتكاس الورم لدى هؤلاء المرضى. كما ينبغي على الجهات المعنية تطبيق إجراءات علاجية مناسبة مع استخدام أساليب تشخيصية فعّالة.
الكلمات المفتاحية: الأورام السدوية المعدية المعوية(تجى آى إس تى), الإنثقاب، إيماتينيب، البطن الحاد، مثبطات التيروزين كيناز(تى كى آى) ,الأمعاء الدقيقة.

1. Introduction

Gastrointestinal stromal tumors (GISTs) are major mesenchymal tumors of the gastrointestinal tract (GIT), medically termed as a neoplasm located in the digestive tract [1]. These originate from interstitial cells of Cajal (ICCs) that are recognized as the pacemaker cells to induce autonomous movement in the GI tract. Its sites of origin are commonly the stomach and small intestine, such as the rectum, appendix, and large and small bowels. Approximately 10-15 cases of GIST per million have been reported globally, common among individuals aged above 60 years. However, the GIST occurrence cases involve a median age of 58 years [2,3]. Moreover, other studies estimated its prevalence at 10-20/1,000 000 population [4,5], and the possibility of malignancy is 20-30% [6]. Alvarez et al. (2024) demonstrated that the majority of patients were affected with small intestinal GIST, recognized as a high incidence in small bowel compared to other GI malignancies [7]. Moreover, 30% of GIST originates from the jejunum and ileum, which are the areas of the small intestine or small bowel [8].

Initially, it has been recognized as a gastrointestinal (GI) autonomic nerve tumor due to the expression of TKI. According to the histochemical observations, the mutation in tyrosine Kinase receptor (TKI) expression and platelet-derived growth factor receptor alpha (PDGFR-α) induce mesenchymal neoplasm, leading to the progression of GIST. This receptor is located at the cell surface of the GI tract lining and is involved in cell-cell communication, cell development, and metabolic mechanisms. [9,10]. Dudzisz-Śledź (2022) mentioned that genetic mutations in TKI and PDGFR- α alter several metabolic pathways, including MAPK signaling, that induce the progression of GIST. In addition, the NF1 gene mutation results in multifocal GIST, inducing gastrointestinal bleeding and anemia in the jejunum or ileum [8].

In the early stages, it has asymptomatic conditions; however, it becomes malignant after its large size and produces abdominal pain. Although, the early growth of GIST in small intestine is the leading source of acute abdomen, causing intraperitoneal hemorrhage, gastrointestinal perforation, and intestinal obstruction [11]. The complex potential of GIST malignancy causes acute abdomen conditions that need an early diagnosis to prevent severe complications through complete resection and chemical therapy such as imatinib [4,12]. Chemical therapy is generally based on the inhibitors of tyrosine kinase (TKIs) used in the treatment of patients with GISTs. Imatinib as a TKI therapy produces various side effects, such as muscle weakness (Anderson syndrome) and tumor recurrence [13]. There are numerous surgical resections, including laparoscopy and endoscopic enucleation, for the diagnosis of GIST, which are applied according to the origin, size, and site of the GIST due to open surgery [14,15]. Small tumors are efficiently managed with complete resection, whereas large-sized tumors have high malignant potential to recurrence despite proper resection, particularly in the case of intraperitoneal infiltration or liver metastasis [16]. Similarly, Vassos et al. (2021) illustrated that a tumor-sized larger than 5cm is the maximum potential of disease recurrence due to high mitotic cell count [17].

Therefore, adjuvant therapies, along with surgical management, contribute to preventing diagnostic challenges of GSI recurrence. The study also highlighted that tyrosine kinase inhibitor (TKI) therapy is required to monitor tumor progression and recurrence during post-surgical resection [18]. Likewise, Hasnaoui et al. (2023) demonstrated that GIST in jejunum has been managed by laparotomy and TKI therapy to reduce the risk of recurrence. Despite extensive care and therapies, the diagnosis of GIST is challenging due to the complex tumor location [19]. However, GIST presented with secondary peritonitis due to perforation usually has a poor prognosis despite surgical resection, followed by adjuvant therapy with TKI Imatinib for at least two years to decrease the recurrence of the tumor [20]. Although, the current research provided extensive literature regarding the surgical management and adjuvant therapies with perforated GIST of the small bowel. Furthermore, it presented a case report along with a literature review for patients with acute abdomen due to secondary peritonitis and perforated small bowel tumors. The research aimed to investigate numerous case reports through literature analysis regarding GIST, along with a case presentation of the patient.

1.2. Case Presentation

A 42-year-old male patient presented with severe generalized abdominal pain, lasting for 6 hours, associated with a history of nausea, vomiting, abdominal distention, pulse rate of 120/min, and 37.8 ○C body temperature. Additionally, an abdominal examination revealed generalized tenderness, board-like rigidity, and sluggish bowel sounds. The patient was diagnosed with acute abdomen and signs of peritonitis. The laboratory tests showed only an elevated white blood cell (WBC) count of 14,000 per microliter and the upright imaging examinations. The thoraco-abdominal radiograph showed air under the Right hemidiaphragm, while transabdominal ultrasonography revealed free fluids in Morisson's pouch and pelvis. Cyto-histopathological examination of the tumor revealed a solid neoplastic mass sized 7×5×4 cm with a locus of surface melting (perforation site of 1.5 cm diameter). Meanwhile, a microscopic examination of the tumor showed two mitotic counts /HPF. In addition, the resected lymph nodes had no alterations, such as infiltration. Further examination, using immuno-histochemistry, was positive for smooth muscle actin, the surface antigens vimentin, S100 protein, proto-oncogene KIT, and CD34, thus suggesting the diagnosis of GIST of the small bowel.

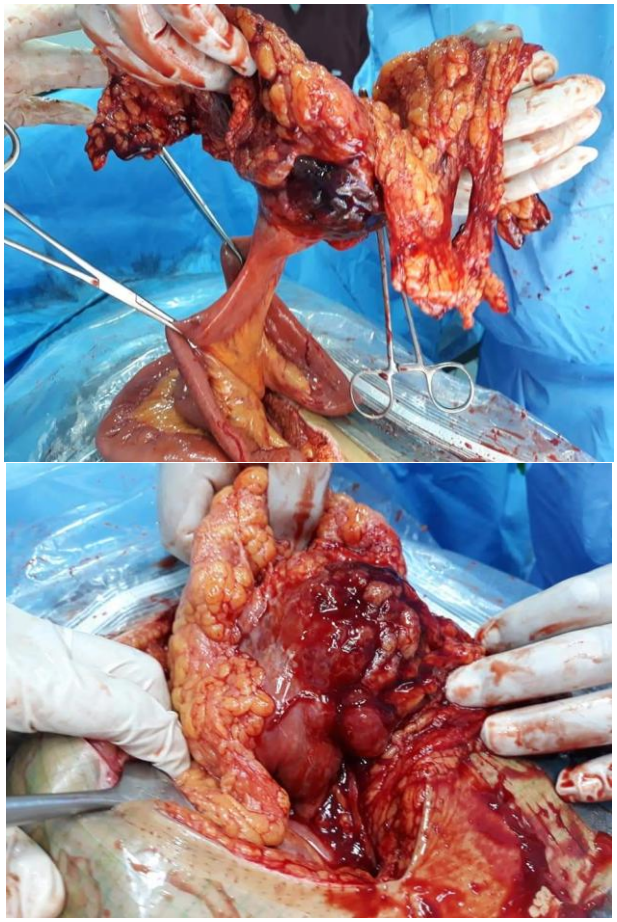

Figure1a and 1b: Perforated Small-Intestinal Stromal Tumor

An urgent explorative laparotomy was performed, which revealed diffuse peritonitis (pus) and a large amount of small bowel content caused by a perforated small intestinal tumor with a maximum diameter of 7-8 cm (Figure 1). The tumor, together with about 10 cm of the jejunum, was resected in an oncological manner with a safe margin, along with regional lymph node excision, and enteroenteroanastomosis were performed. The entire gastrointestinal tract and the peritoneal cavity were examined, and no other abnormalities were revealed. Then, the abdominal cavity was washed with warm, normal saline. Simultaneously, the patient followed the postoperative course and was discharged from the hospital on the 5th postoperative day without complications. Postoperatively, Adjuvant therapy was applied with TKI-Imatinib 300mg tablets twice a day. However, medical treatment was continued for twenty-four months, along with regular follow-ups without disease recurrence (44 months after the operation).

2. Methods

This research employed a literature-based study design to comprehensively assess case reports on gastrointestinal stromal tumors (GIST). The research is based on a systematic analysis of previous literature and case studies through PRISMA analysis, collected from various online research platforms, including the National Center for Biotechnology Information (NCBI) and PubMed, with a duration of August 16, 2010, to December 01, 2024. The research method for databases was used by addressing multiple keywords and search phrases to cover all types of GISTs, such as "Case report on Gastrointestinal stromal tumor."

2.1. Selection of Articles

The selection of articles is comprised of several steps, as shown in Figure 2. Initially, 116 articles were selected by excluding 10 due to duplicates. Further, 70 articles were excluded that were irrelevant to the research inclusion criteria regarding GIST, leaving 36 reports for analysis.

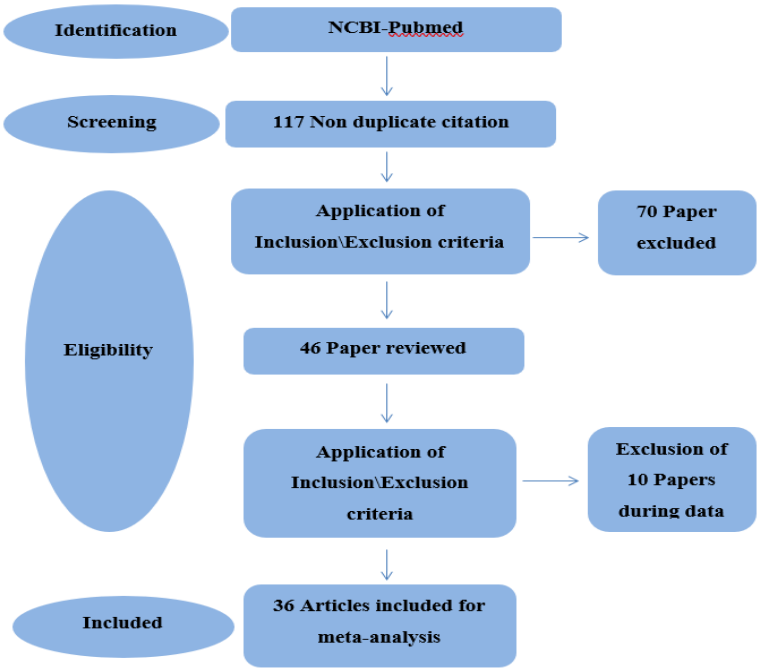

Figure 2: PRISMA Diagram Depicting the Flow of Information Across the Various Phases of a Systematic Review

2.2. Inclusion and Exclusion Criteria

The screening method was utilized to select articles while considering inclusion and exclusion criteria. The articles that were selected were written in English to ensure constant language. The case reports of diagnosed patients with GISTs who belonged to different age groups with unsimilar body weights among males and females were included. The research excluded patients who experienced terminal illnesses, comorbidities, multiple other tumors, and GIST stomach with incomplete follow-ups.

3. Result

Table 1: Clinical Features and an Overview of the Case Reports Presenting Gastrointestinal Stromal Tumor (GIST)

Related Articles						
NO	Article	Age/years	Gender	Complaint	Site	Antibodies expressed
1	Present case (2018)	42 years	Male	Presented to the emergency department (ED) as a case of acute abdomen with severe abdominal pain	Jejunum	vimentin(+), a-SMA(+), CD34(+) and S100 (+) and ,CD117(-)
2	Hashizume et al. (2020) [21]	56 years	Female	Abdominal pain and vomiting	Ileum(Meckel's diverticulum)	CD117(c-kit) (+) and α-smooth muscle actin (+) and CD34 (-), Ki-67 (-)
3	Al-Swaiti et al. (2020) [22]	59 years	Male	severe generalized abdominal pain of four-day duration. Wit 3-month history of weight loss	Jejunum	KIT(CD117)(+), CD34 (+)
4	Enodien et al. (2023) [23]	74 years	Male	Presented with severe, sudden onset lower abdominal pain	Sigmoid colon	CD117 (+) and DOG-1 (+)
5	Chung (2021) [24]	69 years	Female	generalised abdominal pain of 24 h. associated with nausea, vomiting, constipation of 3 days and low-grade fevers, known case of ulcerative colitis,	Jejunum	C-KIT(CD117) (+), CD34(+) DOG1(+)
6	Aldosari et al. (2023) [25]	50 years	Female	generalized abdominal pain, multiple episodes of vomiting, and no bowel	Jejunum	c-KIT(+)

				motion for more than two days		
7	Hosaman et al. (2016) [26]	40 years	Male	complaints of generalized pain in the abdomen for 1 day back	Ileum (Meckel's diverticulum)	C-KIT(+)
8	Badri et al. (2017) [27]	66 years	Male	Abdominal pain and vomiting two days after brain surgery	Small intestine	CD117(+)
9	Behi et al. (2024) [28]	68 years	Male	RIF abdominal pain which progressively worsening over the past 48 h and become generalized. Associated with vomiting and fever. h\o weight loss estimated at 10 kg over 2 months	Terminal ileum	c-KIT(+), CD34(+), and SMA(+), Desmin(-) and S100(-)
10	Yamauchi et al. (2021) [29]	49 years	Female	Abruptly complained of abdominal pain	Transverse colon	KIT(+) DOG1(+) and CD34(+)
11	Sjogren et al. (2013) [30]	39 years	Male	severe chest, abdominal pain after a few months of progressive dyspnea and odynophagia. h\o post prandial emesis and eventually became intolerant of solids and liquids. h\o weight loss over the past few years	oesophgus	KIT (CD117) (+), CD34(+) smooth muscle actin(-) and S-100 protein(-)
12	Patel et al. (2022) [31]	63 years	Male	Severe constant abdominal pain	Ileum (Meckel's diverticulum)	CD117(+) CD34(+)
13	Dev et al. (2024) [32]	53 years	Female	severe, acute abdominal pain and vomiting.	Jejunum	CD117 (+) DOG1 (+)

				O\E Abdominal distension, tenderness, and guarding.		Ki-67 index (-)
14	Furuya et al. (2012) [33]	70 years	Female	Lower abdominal pain	Ileal duplication	c-KIT (+)
15	Lin et al. (2012) [34]	66 years	Male	Severe abdominal pain and vomiting. Gaurding	Small intestine	CD117 (+)
16	Meneses et al. (2020) [35]	46 years	Male	h\o left upper quadrant abdominal pain one day back. h\o fevers and chills.	Proximal Jejunum	c-KIT (+) CD34 (+) pankeratin (-) desmin (-) S100 protein (-) smooth muscle actin (-) Ki-67 index (-)
17	Sato et al. (2017) [36]	74 years	Male	h\o vomiting and abdominal pain for 10 h	Jejunum	c-kit (+) CD34 (+) Ki-67 (-)
18	Patel et al. (2022) [37]	55 years	Male	h\o abdominal pain and diffuse abdominal tenderness	Meckel's diverticulum	CD117 (+) CD34 (+)
19	Li and Jia (2021) [38]	72 years	Female	h\o severe abdominal pain for half an hour and muscular defense over the whole abdomen.	Meckel's diverticulum	CD117 (+) Dog1, SMA and Vimentin (+)
20	Shoji et al (2014) [39]	61 years	Male	Acute abdominal pain and vomiting	Proximal jejunal diverticulum	CD117 (+) CD34 (+)
21	Senti et al (2021) [40]	50 years	Female	acute onset abdominal pain, nausea, and emesis	Small bowel	CD117 antigen (c-kit proto-oncogene) (+) DOG-1 (+)
22	Goyal and Chaudhary (2012) [41]	23 years	Male	h\o fever and pain in the right lower abdomen for the past 2 days	Meckel's diverticulum	CD117 (c-kit), CD 34, smooth muscle actin, and S-100 (+)

23	Yamashita et al. (2014) [42]	72 years	Female	Acute abdominal pain	Sigmoid colon	c-Kit (+)
24	Feng et al. (2010) [43]	45 years	Male	h\o paroxysmal left abdominal pain for 3 days, and persistent pain for 8 hours	Jejunum	tumor derived Vimentin, CD117, CD34, and α-smooth muscle actin (SMA) (+) desmin and S-100 protein, Ki-67 (-)
25	Attaallah et al. (2015) [44]	46 years	Male	h\o vague abdominal pain	jejunum	CD117, DOG1 and bcl-2 and F8 (+) S-100 protein, smooth muscle actin, and CD34 (-)
26	Ueno et al (2014) [45]	72 years	Male	acute abdominal pain	Sigmoid colon	c-KIT and CD34 (+)
27	Arata et al. (2020) [46]	46 years	Male	h\o severe abdominal pain and tenderness and guarding in the upper abdomen	Jejunum	c-KIT and CD34 (+)
28	Fukai et al. (2021) [47]	66 years	Male	h\o severe epigastric pain	Small intestine	c-kit, DOG-1, CD34 and S-100 (-) desmin, alpha smooth muscle actin(SMA) and Ki-67 (+)
29	Ikemura et al. (2015) [48]	82 years	Male	h\o sudden abdominal pain	Ileal diverticulum	c-KIT and CD34 (+)
30	Andican et al. (2010) [49]	48 years	Male	h\o vague abdominal pain lasting for one month	proximal jejunum	C-KIT, smooth muscle actin and S100 (+) desmin and CD34 (-)
31	Sheth et al. (2024) [50]	60 years	Male	4 days of right upper quadrant abdominal pain, nausea,	Oesophagus	c-KIT and CD34 (+)

				nonbloody emesis, nonproductive cough, and chills		
32	Shintaku et al. (2020) [51]	68 years	Male	h\o sudden onset abdominal pain	Sigmoid colon	c-KIT, DOG1, CD34 and Alpha-smooth muscle actin (+) S-100 protein and Ki67(-)
33	Sozen and Tuna (2012) [52]	62 years	Female	presented with peri-umbilical pain that had localized to the right iliac fossa	Meckel's diverticulum	c-KIT and CD34 (+)
34	Chou et al. (2011) [53]	76 years	Female	h\o lower abdominal cramping pain for two days. Episodes of diarrhea and vomiting were noted	Meckel's diverticulum	CD117 and DOG1 (+)
35	Sankey et al. (2015)	70 years	male	h\o abdominal pain for five years.	Jejunum	CD-117 and CD-34 (+)
36	Khuri et al. (2017) [55]	68 years	Female	h\o diffuse abdominal pain 4 hours back, abrupt and sharp. Associated with nausea, recurrent vomiting, and reduced appetite	Proximal Jejunum	CD117, DOG-1 (+) CD34, Desmin, chromogranin, HMB45, and S100 (-)
37	Sreevathsa et al. (2012) [56]	60 years	Female	presented with severe abdominal pain of 5 days duration. associated with P\R bleeding and frequent bilious vomiting lasting for	Caecum	c-kit (+)

				2 days. h\o obstipation for a day prior to admission.		

SMA, smooth muscle antibody; CD, cluster of differentiation; BCL-2, B-cell lymphoma 2; HMB45, human melanoma black-45; DOG-1, Delay of Germination 1; c-kit, tyrosine-protein kinase KIT; Ki67, Antigen Kiel 67; F8, Coagulation Factor VIII

Table 1 tabulates a total of 37 patients in the screened case reports, including 23 (62.2%) males and 14 (37.8%) females, aged from 23 to 82 years, with a mean of 58.35 years. The many patients (62.2%) were older, aged more than 55, and demonstrated that most patients experienced spindle celled tumors sized (6.42 cm) along with maximum mitosis on histopathological examination. Additionally, the immunocytochemistry referred to certain antibodies that have been found in most patients, including CD117, SMA, S100, DOG-1, CD34, and vimentin. According to medical histories, many patients complained of experiencing vague symptoms that may result in negative outcomes of diagnosis. Further complaints were reported, including shock, vomiting, exhaustion, acute severe pain, nausea, or other emergencies.

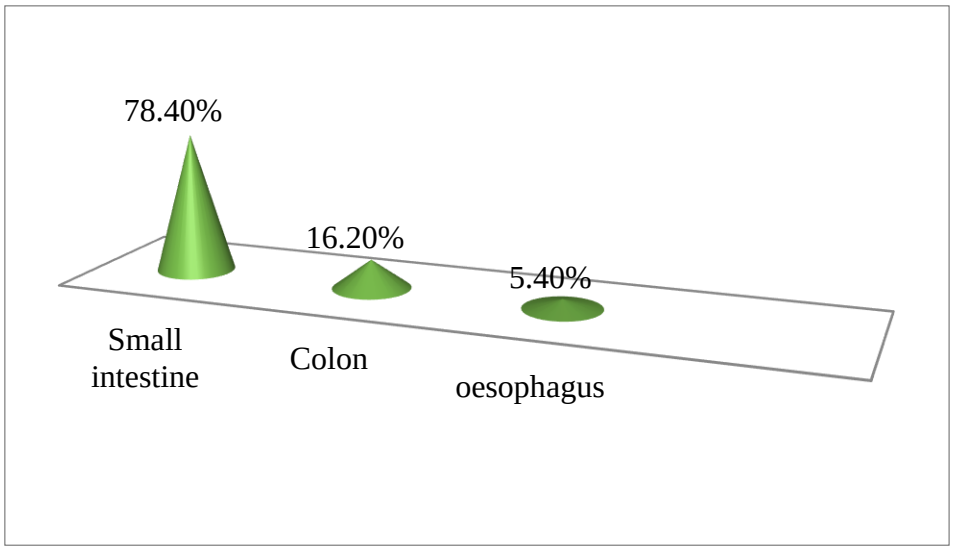

Figure 3: The Percentage of the Research Population's Tumor Sites

Figure 3 demonstrates the percentage of tumor sites in the research population. Most of the case reports have been found on GIST in small intestine (78.40%) compared to colon (16.20%) and esophagus (5.40%).

4. Discussion

The current research investigated numerous case reports through literature analysis regarding GIST, along with a case presentation of the patient. The findings of the study revealed that older individuals are highly affected by GIST along with spindle-shaped tumors. The large size of tumors has been identified across numerous cases that were more than 2 cm, increasing the risk of recurrence. Moreover, the vast cases are based on GISTs in the small intestine, including the site of the jejunum. Generally, the small-sized tumors are less than 2, and large-sized tumors originate from large abdominal masses. These have been discovered earlier or later period as an asymptomatic disease along with a malignancy of 20-30% [4,6]. Several cases revealed the expression of various antibodies among patients, such as CD 117, 34, KIT, and smooth muscle actin. Similarly, antibody expressions are also found in the patient from the current case, along with similar symptoms of acute abdomen pain in previous cases.

For instance, the study of Al-Swaiti et al. (2020) and Chung (2021) showed similar complications of GIST in jejunum with the present case [22,24]. Three are other cases that revealed similar complications in another site of origin, including the Ileum, colon, and esophagus, thus indicating minor differences in symptoms due to tumor

progression [29,30,31]. These cases implemented diagnostic treatment through surgical management along with adjuvant therapies, resulting in positive outcomes except in a few cases. Few cases demonstrated tumor recurrence due to its large size [56]. However, there are also other complications, such as tumor rupture and intraperitoneal migration due to fine needle aspiration at the preoperative stage [4]. Likewise, Hasnaoui et al. (2023) demonstrated that GIST in jejunum has been managed by laparotomy and TKI therapy to reduce the risk of recurrence [19].

Another major factor in GIST diagnosis is the mitotic count, which has been found in numerous previous studies and current case reports. The high mitotic count is the risk factor for recurrent tumors after diagnosis due to the increasing rate of tumor size [17]. Similarly, Fletcher et al. (2002) highlighted the risk of tumor malignancy increases with the high size and maximum mitotic count [57]. The findings revealed the presence of various antibodies at the site of the tumor that may contribute to significant disease markers for its diagnosis, such as TKI protein (CD 117). The TKI receptor is the leading factor of GIST progression due to mutation in its protein synthesis [18,20]. Hence, this study's findings provide insights into the diagnosis through effective markers for the diagnosis of GIST at various sites of origin. Furthermore, outcomes accentuate various factors of tumor recurrence at post-operative stages, facilitating researchers' implementation of effective diagnostic techniques.

4.1. Limitations

1. The research is limited to comprehensive literature of previous case reports along with current cases of GIST patients.

Conclusions

GISTs are the major mesenchymal tumors of the gastrointestinal tract (GIT), which progress due to the mutation in TKI and PDGFR-α receptors. It has asymptomatic conditions however, become malignant due its large size and produce abdominal pain. Several surgical managements have been applied to diagnose patients with GIST, but they increase the risk of recurrent tumors. Therefore, adjuvant therapies contribute to preventing this challenge with several side effects and post-operative complications. This research investigated various previous reports along with the current case regarding GIST. The present case demonstrated diagnosis with complete excision besides lymph node dissection. However, previous cases mentioned antibody expression and mitotic count at the post-diagnosis stage, leading to few negative results. Hence, the research represented the need for effective diagnostic approaches to prevent tumor recurrent rates among diagnosed patients.

5.1. Recommendations

1. Future researchers should address immune markers to reduce tumor recurrence among GIST patients.
2. Stakeholders should implement proper treatment procedures with effective diagnostic methods.

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